BAYER

Fludora® FUSION

A step towards the *future of vector control*

//connect
//combine
// contribute

We're Tackling Resistant Mosquitoes *with a New Approach*

Insecticide resistance is recognized as one of the biggest threats to the gains made in the fight against malaria over the last 15 years. This is largely a consequence of the reliance on a limited number of insecticide classes for vector control. There is therefore an urgent need for new modes of action in malaria vector control as well as new strategies to preserve the effectiveness of both existing and newly available insecticide classes.

At Bayer, we are committed to delivering tools and solutions to address the challenges associated with insecticide resistance. To this end, we are pursuing the development of a completely new insecticide for vector control in partnership with the Innovative Vector Control Consortium. Assuming successful progress through development phases this new insecticide should be available for use in malaria vector control programs within the coming years. However, new modes of action and new approaches are needed now – so we are also investing in making new modes of action available for public health use via repurposed agricultural insecticides.

Given the resistance challenge, all new insecticide classes for public health are precious and their effectiveness needs to be preserved for as long as possible. In the development of the neonicotinoid insecticide class for malaria vector control, we therefore took the approach to focus on a combination product – Fludora® Fusion. It is the first two-way indoor residual spray solution that combines the neonicotinoid clothiandin with a second insecticide with an unrelated mode of action – the pyrethroid deltamethrin.

Our overall aim is to support the capacity of vector control programs to achieve significant impact on diseases via provision of cost-effective solutions that protect more lives.

Fludora® *Concept*

Our Combination

Approach for Effective Vector Control

The approach of using combinations of different modes of action is well-recognized and practiced, both within drug therapies (e.g. ACT anti-malarials) as well as in agricultural crop protection where such combinations can significantly improve the efficacy against resistant pest groups compared to solo insecticides.

We developed Fludora® Fusion based on this principle. Our main objective is to achieve improved efficacy under conditions of insecticide resistance as part of an overall insecticide resistance management strategy.

Fludora® *Fusion*

Discover
the First Two-Way IRS Solution

Fludora® Fusion features two unrelated modes of action for a perfect fit in an insecticide resistance management strategy. This first two-way insecticide combination product enhances the reliability and cost-effectiveness of your IRS program, supporting the objectives to achieve coverage and disease impact.

Product Basics

// **Active ingredients:** Clothiandin (500 g/kg) and deltamethrin (62.5 g/kg)
// **Formulation type:** Wettable powder in water-soluble sachets
// **Packaging:** Water-soluble sachets (100 g or 80 g)
// **Dose rate:** 200 mg/m^2 clothiandin and 25 mg/m^2 deltamethrin
// **Dilution rate:** One 100 g sachet per 10 L sprayer or 80 g sachet per 8 L sprayer
- e.g. 1 kg of Fludora® Fusion fills 10 x 10 L spray tanks
- 20 structures can be sprayed with 1 kg (10 sachets) of Fludora® Fusion (assuming two structures are sprayed per 10 L sprayer)

Key Features and Benefits

// Combination of two unrelated modes of action acting on different target sites; the resulting complementary activity improves robustness of performance under field conditions compared to either active ingredient applied alone.

// Tested and proven effective against more than a dozen resistant strains of mosquitoes, expressing various resistance mechanisms to pyrethroids, carbamates and organophosphates.

// Tested in field trials across 16 countries: these trials indicate an expected residual performance up to 12 months, depending on surface type and mosquito strain.

// The smallest unit-dose sachet size of all currently available non-pyrethroid IRS products, providing the opportunity to further reduce transport and storage costs.

// Available in water-soluble sachets – improving both the convenience of use (easy dilution) and reducing the contamination of the outer packaging.

// High level of safety through reduced product exposure to spray operators.

Our Focus

on Evidence-Based Decision-Making

In recognition of the importance of evidence-based decision making and taking into account the diversity and variability which is inherent in dealing with biological systems, we recognized that results from just a few field trials may not give a complete picture of the likely performance range of Fludora® Fusion across a continent as large as Africa.

To that end we have invested in an unprecedented range of field trials across Sub-Saharan Africa to test and support this position. Fludora® Fusion has been part of a program of 21 field trials across 16 countries from Sub-Saharan Africa. Fludora® Fusion has also been screened across more than a dozen resistant strains to confirm efficacy against known resistance mechanisms.

This trial data set has supported a position of greater robustness and reliability in performance of the Fludora® Fusion combination than was seen with either active ingredient applied alone (and often improved performance compared to current standard products).

Explore Our Latest Insights **from Field Trials**

The following sections are illustrative of cone bioassay results experienced across a range of field trials on different surface types and different mosquito strains.

These results are presented, taking into account the following:

// Cement surfaces tend to be less challenging surface types compared to mud.
// Mud surfaces may vary greatly both between countries but also within countries.
// Trials which included a challenging surface type (like mud) as well as a resistant mosquito strain were more likely to show differences between treatments.
// Clothianidin has a delayed mortality effect and assessments up to 72 hours after cone bioassay exposure are therefore included where necessary.

Our emphasis here is therefore either on the more challenging situations or on simple comparisons of Fludora® Fusion to existing standards. All these results reflect wall cone bioassays as an indicator of residual performance.

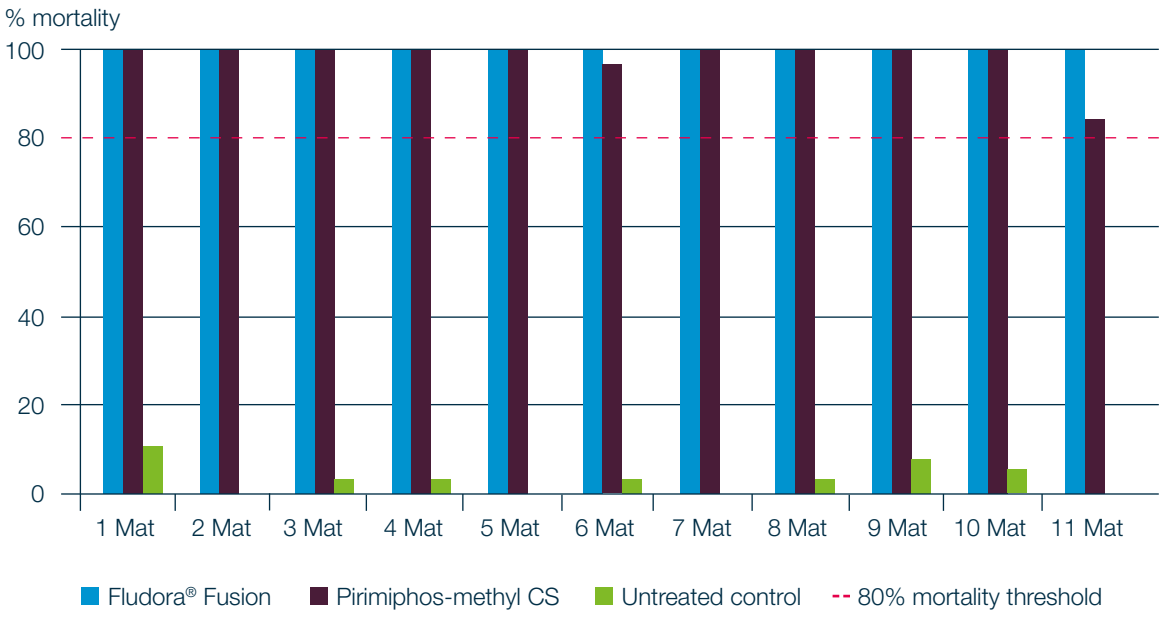
Field Trial Data Summaries

A large volume of trial data has been generated for Fludora® Fusion but only a small selection of that can be represented here. For a more comprehensive view of trial results please contact one of our company representatives to gain access to our online data sharing platform.

Fludora® Fusion Trial Results on Concrete Surfaces – Susceptible Strains

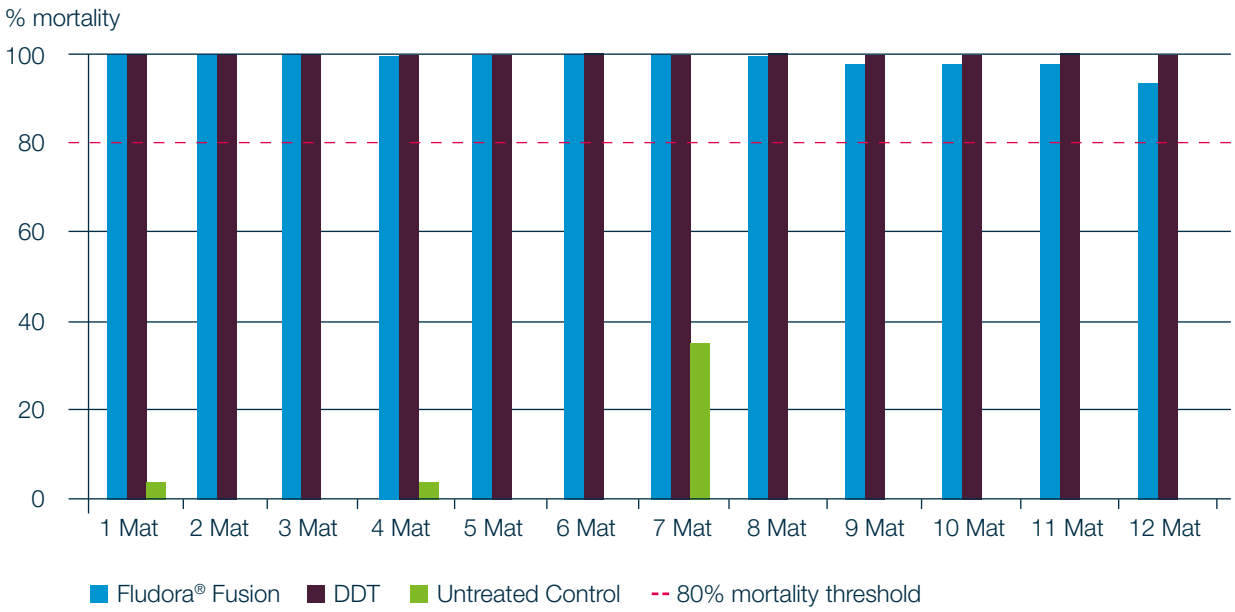
The final results from Rwanda illustrate the potential for Fludora® Fusion to provide season long malaria transmission impact. Fludora® Fusion lasted as long as the current standard Pirimiphos-methyl CS on cement surfaces. It continued to provide 100 percent efficacy until 11 months after spraying when 24-hour mortality from cone bioassays was measured with pyrethroid susceptible mosquitoes.

Residual activity of Fludora® Fusion compared to Pirimiphos-methyl CS on cement walls; results of cone bioassays assessed at 24 hours post-exposure (Pyrethroid susceptible An. gambiae KISUMU strain) (Rwanda, 2017)



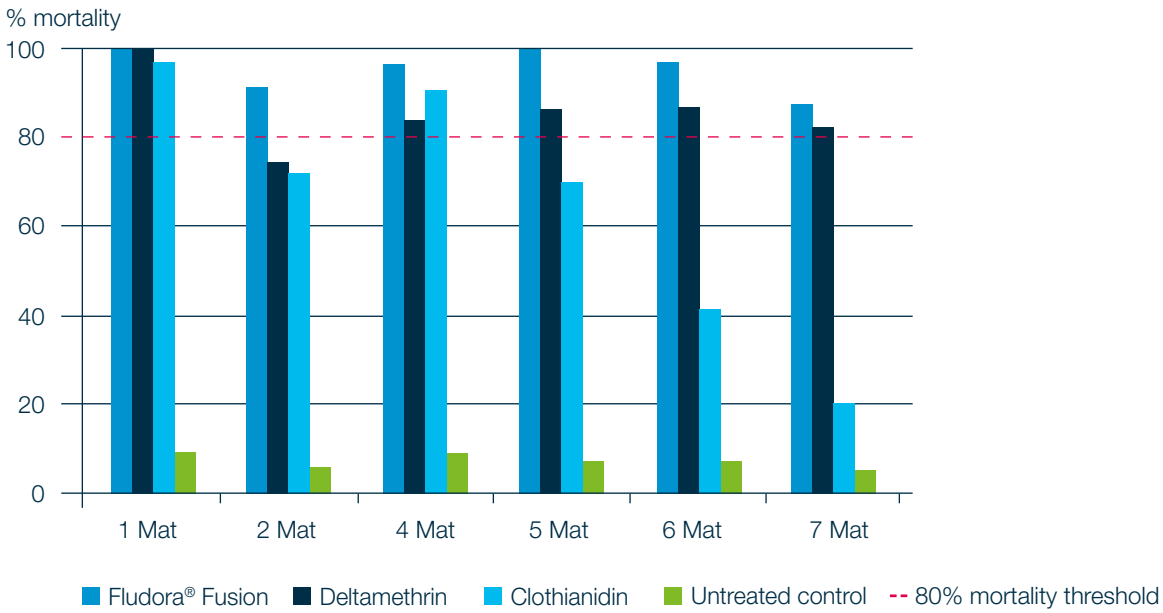
These final results from South Africa also illustrate that Fludora® Fusion has the potential to provide effectiveness spanning a full malaria transmission season. Twelve months of activity, equivalent to DDT, was observed.

Residual activity of Fludora® Fusion compared to DDT-WP on cement walls; results of cone bioassays assessed at 72 hours post-exposure (Pyrethroid susceptible An. gambiae KISUMU strain) (South Africa, 2018)



The **interim** trial results illustrated below established in Southern Ghana by the Noguchi Institute show residual activity above the 80 percent threshold at seven months after spraying. The Fludora® Fusion combination outperformed the individual insecticide components.

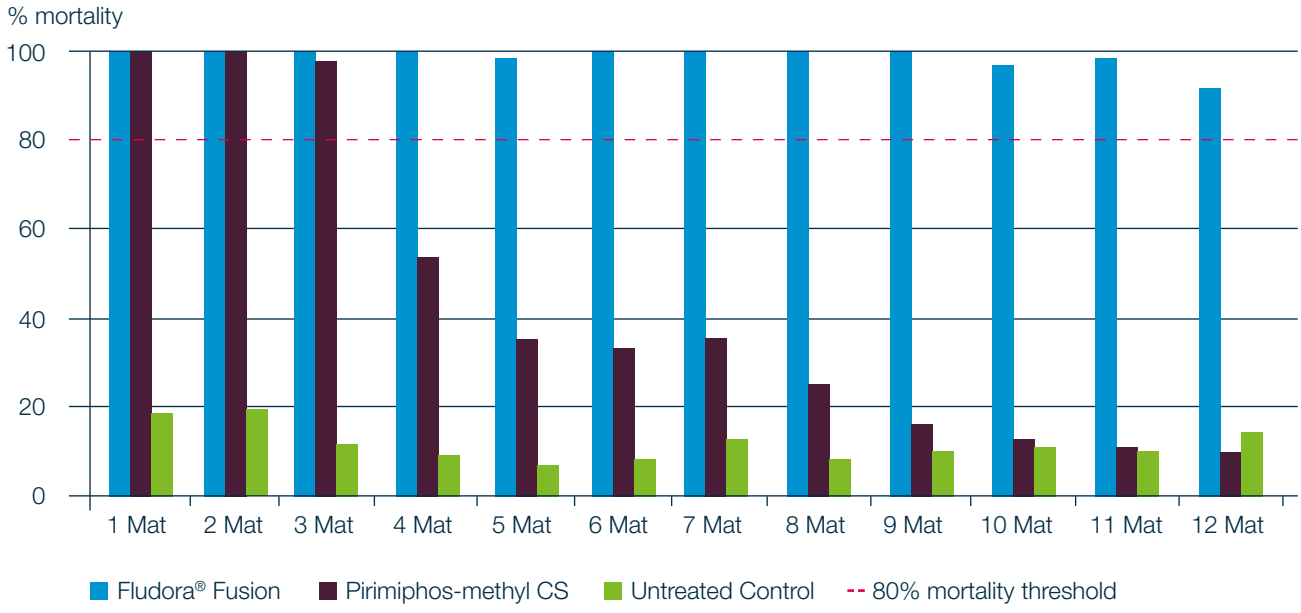
Interim results: Residual activity of Fludora® Fusion compared to individual insecticide components on cement surfaces against susceptible An. gambiae KISUMU in wall cone bioassays at 72 hours post-exposure (Noguchi Institute, Ghana, 2017)



Fludora® Fusion Trial Results on Mud Surfaces – Susceptible Strains

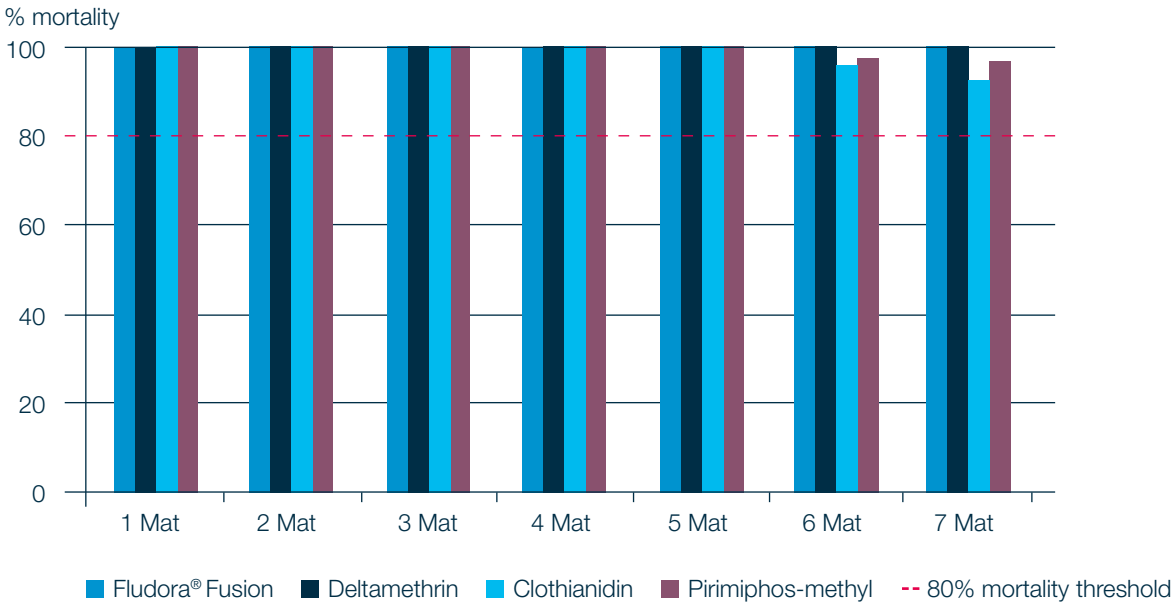
In this trial carried out in Northern Zambia, Fludora® Fusion provided residual activity, as measured by cone bioassays, above the threshold of 80 percent for a period of 12 months on mud surfaces against a pyrethroid susceptible strain. Fludora® Fusion outperformed the current standard of Pirimiphos-methyl CS.

Residual activity of Fludora® Fusion, compared to Pirimiphos-methyl CS on mud surfaces against pyrethroid-susceptible An. gambiae KISUMU strain in cone biossays at 72 hours post-exposure (Not corrected for control mortality) (TDRC, Zambia, 2017)



The **interim** results from our field trial in Tanzania show that Fludora® Fusion (and other treatment arms) continued to provide acceptable levels of control, above 80 percent mortality threshold, at the seven-month assessment point as measured at 48 hours post-exposure.

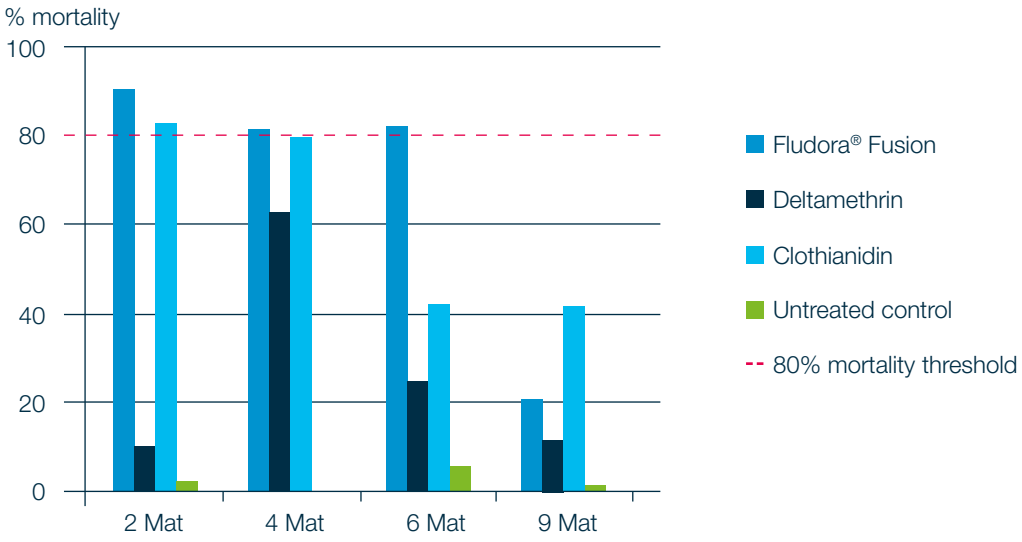
Interim results: Residual activity of Fludora® Fusion on mud surfaces against susceptible strain An. gambiae s.s. in experimental hut wall cone biossays – Mortality at 48 hours post-exposure (Tanzania TPRI, 2017)



Fludora® Fusion Trial Results on Mud Surfaces – Resistant Strains

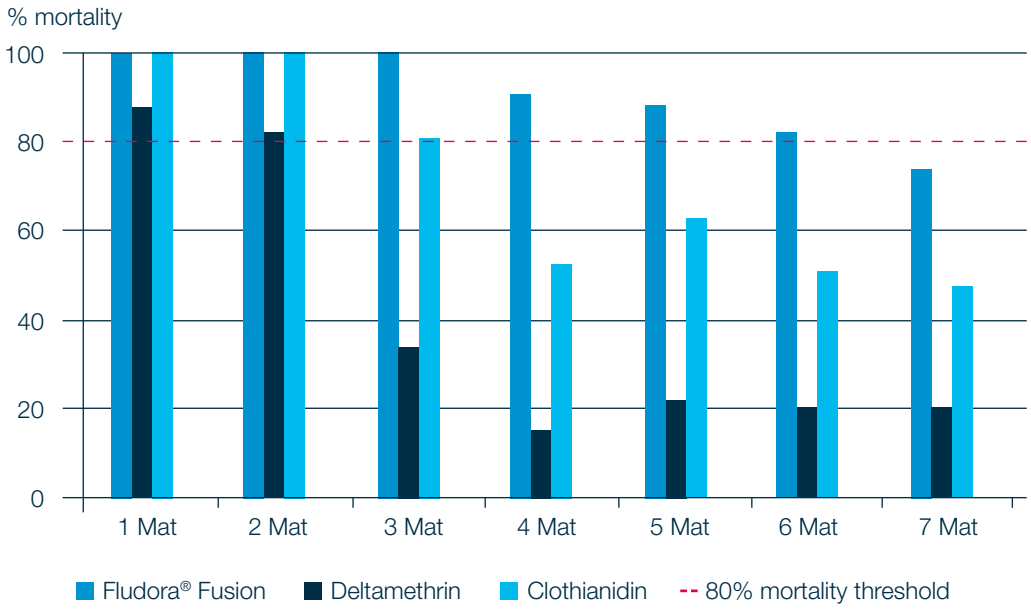
In this small-scale village trial, Fludora® Fusion continued to provide efficacy above the 80 percent threshold against wild pyrethroid resistant strains for a period of six months on mud surfaces, this result was better than either component applied alone.

Residual activity of different insecticides on smooth mud surface against wild pyrethroid resistant mosquitoes in wall cone biossays – 72 hours holding time (CREC Benin, 2016)



In this experimental hut trial, the **interim** results of the cone bioassays showed six months of activity of Fludora® Fusion on mud surfaces against wild resistant strains. This performance was better than the individual components applied alone (even taking into account 120-hour post-exposure mortality for clothianidin alone).

Residual activity of Fludora® Fusion and individual component insecticides on mud surface against a wild pyrethroid resistant mosquito strain from Mbé, Cote D'Ivoire in cone biossays (assessed at 120 hours post-exposure) (LSHTM, 2016)

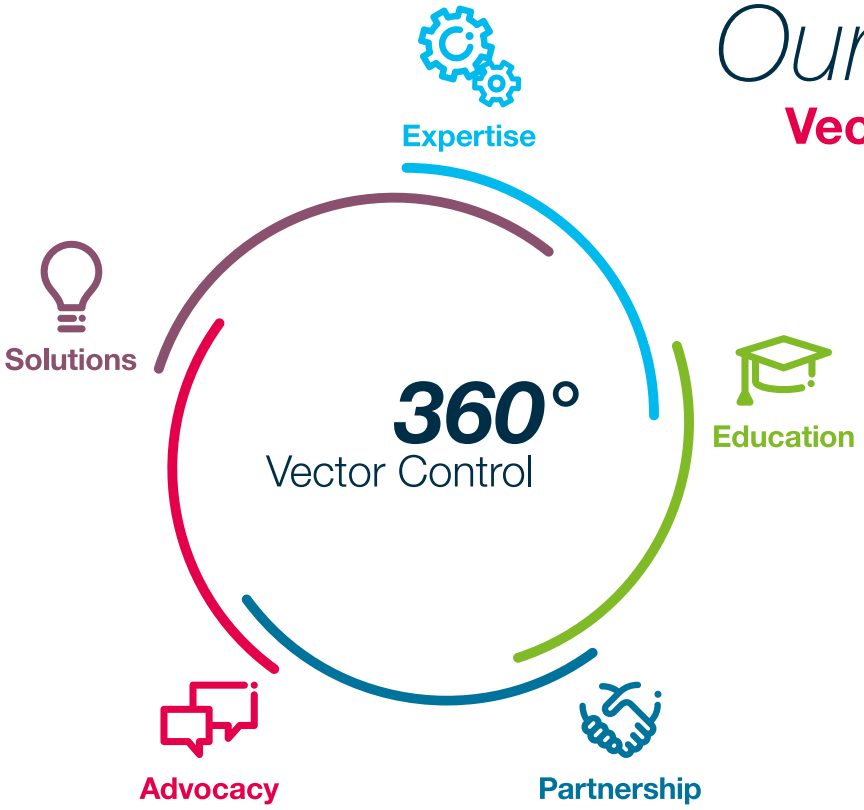


Fludora® Fusion

Availability

Fludora® Fusion is included on the list of WHO prequalified vector control products. Registrations have been achieved in 18 countries in Sub-Saharan Africa so far, with more pending.

We intend to make Fludora® Fusion available at a price which supports the objective to increase coverage of IRS. We use a metric of 'cost per household per month of activity' as a benchmark reference point and we intend to achieve the lowest cost per household per month of activity compared to other newly developed IRS formulations.



Our 360°
Vector Control Vision

We have been contributing to the fight gainst vector-borne diseases for over 60 years. This experience has supported our perspective that achieving impact with vector control needs a holistic approach beyond product solutions. We put this into practice with our 360° Vector Control strategy:

Expertise: Recognizing the importance of both sharing our own expertise and learning from others ensures that our innovation resources are well directed and that we can provide relevant training and stewardship support where needed – to improve the health and quality of life in communities around the world.

Education: We use our resources to provide training relevant to product usage, safety and insecticide resistance management but complement that with online educational tools and support to universities.

Partnership: We reflect the old proverb 'If you want to go fast, go alone, if you want to go far, go together'. Our focus on strong collaborative partnerships with a number of organizations is with the view of long-term sustainability of impact against vector-borne diseases.

Advocacy: We contribute our voice to advocating for awareness and support to the fight against vector-borne diseases in unison with other organizations committed to the same cause.

Solutions: Our current and pipeline portfolio of vector control solutions are designed to address relevant challenges and needs within the scope of vector-borne diseases.

For more information, visit **www.vectorcontrol.bayer.com**

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